during the last month of treatment. **RESULTS:** Of 167 patients (20 men, 147 women; mean age 43.5 years) included in the analysis, 72% responded to tegaserod. At baseline, SF-36 scores from IBS-C patients were lower than those from the general population, but increased in all dimensions with treatment ($p = 0.0068$ for General Health), reaching values similar to those of the general population. An increase in all SF-36 dimensions was observed in responders (R), whereas a decrease occurred in non-responders (NR, General Health dimension $p = 0.004$). IBS-QOL scores (from baseline to treatment) significantly increased in all dimensions ($p < 0.0001$ for overall assessment). The mean increment in IBS-QOL was greater for R than NR (Overall dimension, $p < 0.05$). Upon treatment withdrawal, some dimensions of SF-36 and IBS-QOL scores decreased but did not return to pretreatment levels. **CONCLUSIONS:** QoL is impaired in IBS-C patients. Treatment with tegaserod 6 mg b.i.d. improves QoL in patients with IBS-C to a level almost equivalent to that of the general population, and deterioration in QoL occurs upon treatment discontinuation.

METHODS & CONCEPTS

PMC1

USE OF THRESHOLDS FOR SAFETY REPORTING IN CLINICAL TRIALS

Frame D, Fahrbach K, Reynolds MW, Ross SD
MetaWorks Inc, Medford, MA, USA

OBJECTIVE: To assess completeness of safety reporting in published clinical trials, including use of incidence, severity, and relationship to drug thresholds for listing of specific adverse events (AEs). **METHODS:** We used data from previously conducted systematic reviews in three areas: treatment of rheumatoid arthritis (RA) with disease-modifying anti-rheumatic drugs (168 studies, 1969–2001); treatment of migraine with 5HT-1 agonists (38 studies, 1991–2003); and anti-neoplastic treatment of relapsed or refractory non-Hodgkin's lymphoma (NHL) (27 studies, 1991–2003). The type of safety reporting for each study was appraised by two reviewers. **RESULTS:** Only a minority of studies in each of the clinical areas presented a complete listing of all AEs occuring during the trial (RA 17%, migraine 8%, NHL 30%); a substantial number (10–25%) had no safety data extractable. Among studies with partial AE reporting the thresholds used varied by clinical setting: two-thirds of RA and NHL studies with a reporting threshold used the author- or investigator-attributed relationship to drug to determine which AEs would be listed in published reports, while 71% of migraine studies with a threshold used incidence (e.g. only AEs occuring in more than 5% of patients were listed). The severity threshold (reporting of only serious AEs or only grade 3–4 AEs) was the least common in all three clinical areas examined. No consistent relationship was found between complete AE reporting and study sponsorship (industry vs. non-industry/not reported) or year published (pre vs. post 1995). Smaller studies (<100 patients) were more likely to contain complete AE reporting, perhaps due to the difficulty of providing a comprehensive listing of all events in larger studies. **CONCLUSIONS:** Incidence and relationship to drug remain common thresholds for AE reporting in published clinical trials. Early detection of rare or unanticipated events by meta-analysis of published trial data is thus made more challenging.

PMC2

A SYSTEMATIC REVIEW OF ECONOMIC EVALUATIONS OF GENETIC TESTING TECHNOLOGIES

Ramsey S[1], Henrikson N[2], Carlson J[2], Veenstra DL[2]
[1]Fred Hutchinson Cancer Research Center, Seattle, WA, USA;
[2]University of Washington, Seattle, WA, USA

Genetic test technologies offer hope for early diagnosis and identification of persons at risk for serious diseases. Because many of these tests are costly and applicable to large populations, evaluations of the cost-effectiveness of these technologies are important. **OBJECTIVES:** To conduct a systematic search for and review of economic evaluations of genetic testing technologies. **METHODS:** PubMed, Proquest, LexisNexis, Expanded Academic Index, The Harvard Review of Economic Analyses, PsyclINFO, NICE and CCOHTA databases were searched for original cost-effectiveness articles published from 1990 to present. MESH terms included: economic(s) and/or cost(s), genetic, gene, and/or genotype. Selection criteria included genetic tests for genetic conditions, defined as analysis of human DNA, RNA, chromosomes, proteins, and certain metabolites in order to detect heritable disease-related genotypes, mutations, phenotypes or karyotypes for clinical purposes. Articles were categorized by clinical category and type of economic study (e.g., cost-utility, cost-benefit), then graded independently by the authors using CEA study quality system developed by Chiou et al (Med Care, 2003;41:32). **RESULTS:** A total of 149 abstracts were retrieved using the search terms; 63 met selection criteria. Types of economic studies were as follows, cost-utility (25%); cost-benefit (19%); cost-minimization (6%); cost-effectiveness (59%). Clinical testing categories were as follows: preconception carrier (8%); prenatal diagnosis (40%); adult (57%). The studies involved 26 different medical conditions. Study quality ranged from 43–100 (average 82). Cost-utility studies were of highest quality (mean 91); cost-minimization studies were of lowest quality (mean 63). Adult studies had the highest rating (mean 86); preconception testing studies were lowest in quality (mean 74). Intraclass correlation among raters was 0.82 (CI 0.70–0.89). **CONCLUSIONS:** A number of economic analyses have been published in human genetics across a wide range of conditions. Study quality varied widely. Priority areas for the field include increasing quality and uniformity of measures of outcome.

PMC3

INTRODUCTION OF BIAS WHEN USING THE SMEARING RE-TRANSFORMATION METHOD IN THE PRESENCE OF POSITIVELY SKEWED ANTI-LOGGED RESIDUALS

Wang MT, Malone DC, Skrepnek GH, Armstrong EP
University of Arizona College of Pharmacy, Tucson, AZ, USA

OBJECTIVES: The purpose of this study was to evaluate the effects of using Duan's mean anti-logged residuals (mean smearing estimator) or a median smearing estimator with positively skewed distributions on predicting costs. **METHODS:** Data for this study came from managed care pharmacy and medical records containing drug-drug interactions (DDIs) from January 1, 1997 to December 31, 1999. Two matched cohort groups were studied. DDI cases were identified as receiving medications involving monoamine oxidase inhibitor (MAOIs) or anti-coagulant DDIs. Controls were age and sex matched to cases. Costs were positively skewed and were then natural log transformed as the dependent variable in regression models. The retransformed costs employing the mean and median smearing estimators, respectively, were compared. Model fit was assessed using mean squared error (MSE) for both mean and median smearing estimators. **RESULTS:** A total of 156 and 5754 subjects were identified as MAOI and anti-coagulant groups, respec-